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Interventions for reducing sedentary behaviour in people with stroke

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To determine whether interventions primarily intended to reduce time spent in sedentary behaviour after stroke reduce sedentary time, and whether they modify cardiovascular risk, and reduce the risk of death or secondary vascular events. We will also include interventions intended to reduce the length of prolonged uninterrupted periods of sedentary behaviour (i.e. interventions to fragment or interrupt).

Primary objectives

To determine whether interventions to reduce or interrupt sedentary time influence:

- mortality;
- recurrent cerebrovascular or cardiovascular events.

Secondary objectives

To determine whether interventions to reduce or interrupt sedentary time influence:

- amount of sedentary time;
- cardiometabolic risk profile (e.g. glucose tolerance, arterial function, blood cholesterol and blood pressure);
- adverse events (in addition to recurrent events, for example falls).

Other objectives

In addition, we will as a scoping exercise, describe the range of all outcome measures reported in all trials. By definition, any included study interventions will fall within the umbrella of physical activity. Therefore, it may be that multiple plausible benefits could emerge that are common to other energy-expending interventions.

BACKGROUND

Interventions to increase physical activity, including exercise, are routinely included in recommendations for stroke rehabilitation and secondary prevention; some also include a recommendation for reduced sedentary behaviour (Billinger 2014). However, little is known about the effectiveness of interventions to reduce sedentary behaviour after stroke. There is growing public health concern about the effects of sedentary behaviours (Chau 2013; Young 2016).

The Sedentary Behaviours Research Network (SRBN) Terminology Consensus Project (Tremblay 2017) defines sedentary behaviours as “any waking behaviour characterized by an energy expenditure ≤ 1.5 METS (metabolic equivalents; Ainsworth 2011) while in a sitting, reclining or lying posture”.

An underlying assumption in this definition is a lack of muscle activity in the large muscle groups that contribute to the weight bearing of the body during a sitting or reclining posture (Tikkanen 2013). A lack of muscle activity leads to suppression of skeletal muscle lipoprotein lipase (LPL; Hamilton 2004). Reduced LPL activity is linked to decreased levels of high-density lipoprotein (HDL)-cholesterol, increased triglycerides levels (Pesola 2015), insulin resistance and glucose intolerance (Bergouignan 2011) and increased risk of all-cause mortality (Thomsen 2014). Therefore, the amount of muscle activity seems to be an important (implicit) factor of the sedentary behaviour definition and has to be taken into account when identifying sedentary behaviour. Sitting is the predominant wake-time sedentary behaviour, and therefore is often the target for measurement and intervention efforts to reduce sedentary behaviour. Indeed, many of the monitors used to objectively measure sedentary behaviour do not readily distinguish between sitting and reclining postures (e.g. activPAL3™).

Too much total time spent sedentary is associated with poor health, including elevated cardiometabolic risk markers, type 2 diabetes and premature mortality (Biswas 2015; Matthews 2012); the effects are observed in studies that control for levels of physical activity; that is, they are independent of physical activity. A recent large meta-analysis of over one million participants demonstrated that the negative effects of sedentary behaviours (sitting time) on health are most pronounced for people in the highest quartile of sitting time (more than eight hours per day) and the lowest quartile of physical activity (less than 2.5 MET hours per week; Ekelund 2016). High sitting times are particularly damaging:

- when sitting for more than 10 hours per day (Pandey 2016);
- when accumulated in prolonged uninterrupted bouts (Healy 2008; Healy 2011);
- when combined with low levels of physical activity (Biswas 2015; Bouchard 2015).

Therefore, interventions to reduce sedentary behaviour could benefit cardiovascular risk and mortality in a range of patient populations including people with stroke.

Description of the condition

A stroke is caused by an interruption to the circulation of the brain, either by a clot (ischaemic stroke) or a bleed (haemorrhagic stroke). The classic definition of stroke is “rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin” (Hatano 1976). Globally, stroke is the second leading cause of death and third leading cause of disability adjusted life years (World Health Organization 2016), with around 50% of stroke survivors experiencing long-term disability (Mackay 2004). The average age-standardised incidence of stroke in high-income countries significantly decreased by 12% between 1990 and 2010. Over the same period, stroke incidence showed a non-significant increase of 12% in low- and middle-income countries, where the burden of stroke was greatest (Feigin 2014).

Risk factors

Global risk factors for stroke include hypertension, elevated blood lipids, diabetes, atrial fibrillation, and modifiable lifestyle factors, including physical inactivity, poor diet, obesity, smoking and alcohol (Kuklina 2012). The key risk factors, for first or recurrent stroke, are cardiometabolic in nature and include hypertension (Sacco 1997), and impaired glucose tolerance (Fonville 2014). Prediabetes is present in 23% to 53% of stroke and transient ischaemic attack (TIA) survivors and is responsible for a two-fold increase in the risk of recurrent stroke (Fonville 2014). The increased cardiovascular risk and mortality after stroke could be contributed to by sedentary behaviours coupled with inactivity.

Recurrent stroke

Recurrent stroke is common among those who survive the initial index stroke event. Systematic review data demonstrates the cumulative risk of stroke recurrence is 3.1% at 30 days, 11.1% at one year, 26.4% at five years, and 39.2% 10 years after the index stroke event (Mohan 2011). While there is some evidence of longitudinal decline in stroke recurrence, this remains a major clinical issue with a third of patients having secondary strokes or being dead within five years (Pennlert 2014). Secondary stroke prevention, for example by reducing sedentary behaviour and increasing physical activity after stroke, is, therefore, of paramount importance.

Sedentariness and inactivity

Many stroke survivors are both sedentary (i.e. sit for long periods each day) and physically inactive (i.e. do not meet guidelines for moderate to vigorous physical activity (MVPA; Bull 2010), even those who have the physical capability to be more active (Tieges 2015). There are a number of studies that demonstrate the nature of these issues in people with stroke.

- Observational studies have objectively measured sedentary behaviour (sitting time) in stroke survivors living at home and show stroke survivors typically sit for more than 10 hours per day (English 2015; Kerr 2015; Kunkel 2015; Paul 2016; Tieges 2015). This falls within the category of concern identified by Ekelund 2016.
- Sitting time is known to remain high for at least the first the year after stroke. Sedentary time exceeding 10 hours per day has been observed immediately post-discharge (Kerr 2015), one year post-stroke (Kunkel 2015; Tieges 2015) and several years post-stroke (4.2 ± 4.0 years: Paul 2016; and 4.4 ± 10 years English 2015).
- High sitting time after stroke includes a pattern of prolonged, uninterrupted bouts of sedentary time (median bout length 1.7 hours (interquartile range (IQR) 1.4 to 2.2; Tieges 2015).
- People with stroke also tend to be physically inactive. A recent systematic review (including 26 studies and involving 983 participants) demonstrated that among community-dwelling stroke survivors' step counts are less than 50% of age-matched controls and sedentary time occupies 63% to 87% of reported monitoring periods (English 2014).
- People with stroke spend less time daily in light physical activity and MVPA in comparison with age-matched healthy control participants (English 2015); people with stroke spent 4.9 (standard deviation (SD) 5.8) minutes per day, whilst control participants spent 38 (SD 31.0) minutes per day in MVPA. Failure to achieve regular adequate levels of MVPA places stroke survivors at even higher risk from the effects of high sitting time (Ekelund 2016).

The reasons why stroke survivors tend to be physically less active and more sedentary than their healthy counterparts are beginning

to be better understood. First, lack of physical activity may be one of the risk factors that precipitates stroke in a proportion of cases, and where this is a habit that may be difficult to change after stroke. Findings from qualitative studies (Morris 2015; Morris 2017; Nicholson 2014), and systematic reviews (Morris 2012; Nicholson 2013), have highlighted a range of barriers to increasing physical activity after stroke. These relate to stroke survivors themselves (e.g. fear of another stroke, fatigue, depression), carers (e.g. lack of confidence), professionals (e.g. perceived role limitations), and the environment (e.g. lack of appropriate access). Interventions that included tailored counselling to reduce these barriers were more effective in increasing the uptake and maintenance of physical activity after stroke than supervised exercise alone (Morris 2015). The effectiveness of interventions aimed at changing sedentary behaviour after stroke is, however, yet to be established.

In summary, prolonged uninterrupted periods of sedentary behaviour (sitting) occurs alongside the low levels of physical activity common after stroke: a pattern which persists long term. This could contribute to the long-term high risk of secondary cardiovascular events and death observed among stroke survivors. Therefore, interventions to reduce or interrupt sedentary time, or both, as well as increase physical activity at any time post-stroke, are of paramount importance to reduce the global burden of stroke.

Description of the intervention

Interventions to influence sedentary behaviour require behaviour change strategies, a taxonomy of which was provided by Michie 2013. A recent review clarifies the effectiveness of different behaviour-change strategies used in interventions to reduce sedentary behaviour (Gardner 2016; more than 50% of the interventions reviewed were work-site based). The review authors suggest that interventions incorporating changes to environment (social and physical), self-regulatory techniques (self-monitoring and problem-solving) and provision of health information were connected to effectiveness. Therefore, interventions to reduce (or interrupt) sedentary behaviours after stroke could vary greatly in nature. Possible behavioural interventions could include, but not be limited to:

- prompting mechanisms to interrupt prolonged sitting (e.g. mobile phone apps or wearable fitness devices);
- provision of information about health consequences (e.g. effects of sedentary behaviour, physical activity and inactivity);
- provision of feedback on behaviour (e.g. devices to demonstrate the amount of time people have spent sitting);
- action planning (e.g. prompting a person on when they might sit less at a particular time on a certain day);
- restructuring the physical home environment to encourage standing or moving (e.g. cushions that offer vibratory feedback on time spent sitting, furniture for sitting, TV lockout mechanisms, restricting use of remote controls and labour-saving devices)

- facilitating walking in place of seated transport.

Sedentary time reduction need not explicitly be restricted to behavioural interventions. It is also plausible that pharmacological interventions with the potential to reduce fatigue (e.g. caffeine or Modafinil) could be provided with the intention of reducing sedentary time.

Two recent systematic reviews have examined the effectiveness of interventions to reduce sedentary time in adults (Martin 2015; Prince 2014); neither included cohorts of people with stroke. One of these focused on interventions targeting physical activity or sitting time, or both, in adults (Prince 2014: 63 studies, 446 participants). Martin 2015 (51 studies, 8087 participants) included a broader range of potential interventions comprising those specifically intended to reduce sitting time (3/51), interventions aimed at increasing physical activity (16/51), interventions combining sitting time reduction with increased physical activity (9/51), dietary interventions (1/51), and multi-component lifestyle interventions (22/51).

Gardner 2016 suggests that interventions targeting sedentary behaviour rather than increasing physical activity may be more effective. Conversely, there are good reasons why replacing sedentary behaviours with physical activity/exercise after stroke may provide not only additional advantage not just for cardiovascular disease (CVD) risk and mortality (Ferreira 2016), but also multiple cognitive, physical, and psychosocial benefits (Saunders 2014). Also, high levels of moderate intensity physical activity (i.e. about 60 to 75 minutes per day) seem to ameliorate the increased risk of death associated with high sitting time (Ekelund 2016). However, because achieving adequate MVPA is difficult for stroke survivors, reducing sedentary time might be a more achievable target for secondary prevention in many stroke survivors. Therefore, interventions to reduce sedentary behaviour could be widely applicable after stroke because they could be used by stroke survivors who find physical activity difficult, and still be implemented alongside physical activity and exercise interventions for those who are more high functioning.

In summary, interventions for reducing sedentary time may be complex in nature, comprising a number of 'active ingredients', and they may be achievable and relevant for a wide range of people with stroke - including those who are non-ambulatory.

How the intervention might work

Recent systematic review evidence demonstrates that interventions to target sitting time among adults are effective in reducing total sitting time (Martin 2015). Evidence of intervention effects on changes in patterns of accumulation of sitting time remains limited. These behavioural interventions seem feasible in adults and, if the effects on sitting time can be replicated in people with stroke, this could trigger benefits which are clinically important as well as meaningful for people with stroke.

Risk reduction

In people with stroke high sedentary time is prevalent (English 2015; Kerr 2015; Kunkel 2015; Paul 2016; Tieges 2015), and high sedentary time is associated with increased cardiometabolic risk (Biswas 2015; Matthews 2012). Therefore, it can be hypothesised that interventions that reduce sedentary time after stroke could improve the profile of cardiometabolic risk, which, in turn, could reduce the chance of vascular events (including recurrent stroke) and reduce mortality. For example, hypertension is the most important cardiometabolic risk factor for first and recurrent strokes (Sacco 1997). Increased time spent in sedentary behaviours is associated with increased blood pressure (Lee 2015). Reducing systolic blood pressure (SBP) by 5 mmHg causes a 10% reduction in the risk of cardiovascular and cerebrovascular events (including stroke BLTTC 2008).

In other populations, including overweight and obese, diabetic and pre-diabetic populations, laboratory-based studies have shown positive, short-term effects of breaking prolonged sitting time on cardiovascular disease risk factors, such as postprandial hyperglycaemia (Bailey 2015; Dempsey 2016; Dunstan 2012, Henson 2015; Holmstrup 2014; Peddie 2013), plasma clotting factors (Howard 2013), blood pressure (Larsen 2014), and possibly endothelial shear forces (Thosar 2015). However, the long-term effectiveness of reducing sedentary time remains largely unknown.

Other benefits

Reducing sedentary time necessarily (by definition) involves replacing it with some form of physical activity. Therefore, numerous plausible, meaningful benefits could be achieved though reducing sedentary time; these may be similar in nature to other interventions that aim to increase energy expenditure, including physical activity and exercise. Even the demands of simply rising from sitting in a chair should not be underestimated. Sit-to-stand transitions themselves increase metabolic energy expenditure by approximately 35% above resting levels (Júdice 2016), and recruit 78% to 97% of maximal muscle strength in older people (Hughes 1996): this represents substantive high-intensity muscle contraction and effort. Therefore, the most basic element of interventions to reduce or fragment sitting time could, in itself, result in benefits resembling those expected from physical activity and even exercise. This means a broad range of benefits might occur for people with stroke including those relating to physical function, complications of immobility (Govan 2007), and cognition (Cumming 2012). Importantly, interventions to interrupt sedentary behaviour (e.g. assisted sit-to-stand transitions) may be feasible for stroke survivors who are non-ambulatory. There are good reasons why a range of multiple, meaningful benefits could arise from interventions to reduce sedentary behaviour after stroke in the same way that they do for physical activity and exercise interventions (Saunders 2014).

Why it is important to do this review

As described earlier, recurrent stroke (and death) are very common after stroke (Mohan 2011; Pennlert 2014). Interventions to avoid recurrent stroke are ranked among the 'top 10 research priorities for life after stroke' by stroke patients and their carers (Pollock 2014). Sedentary behaviour is a common and persistent feature of life after stroke (English 2015), and this is likely to have a negative impact on cardiovascular risk factors which increase the chance of recurrent strokes and death (Ekelund 2016).

Therefore, interventions that reduce/interrupt sedentary behaviours may reduce cardiovascular risk factors and reduce the chance of recurrent strokes and death for a large proportion of stroke survivors. It is also plausible that interventions that reduce sedentary behaviour may also ameliorate some common complications of immobility (Govan 2007), and could benefit cognitive function, which is ranked highest among the 'top 10 research priorities for life after stroke' as identified by stroke patients and their carers (Pollock 2014).

Reducing sedentary behaviour is currently recommended within guidelines for physical activity and exercise after stroke (Billinger 2014). However, the benefits (and risks) of this after stroke have not been established or explored using rigorous systematic review methodology.

Currently, we do not know if sedentary behaviour can be reduced effectively after stroke and whether doing so has an impact on adverse events. If sedentary behaviour can be reduced after stroke, we do not know whether cardiometabolic risk is reduced and whether benefits to secondary prevention and mortality occur.

The findings of this review will:

- inform development of new trials and interventions;
- add to future iterations of the physical activity and exercise guidelines for people after stroke;
- inform clinical practice;
- inform education and training of health, social care, and exercise professionals working with people with stroke.

OBJECTIVES

To determine whether interventions primarily intended to reduce time spent in sedentary behaviour after stroke reduce sedentary time, and whether they modify cardiovascular risk, and reduce the risk of death or secondary vascular events. We will also include interventions intended to reduce the length of prolonged uninterrupted periods of sedentary behaviour (i.e. interventions to fragment or interrupt).

Primary objectives

To determine whether interventions to reduce or interrupt sedentary time influence:

- mortality;
- recurrent cerebrovascular or cardiovascular events.

Secondary objectives

To determine whether interventions to reduce or interrupt sedentary time influence:

- amount of sedentary time;
- cardiometabolic risk profile (e.g. glucose tolerance, arterial function, blood cholesterol and blood pressure);
- adverse events (in addition to recurrent events, for example falls).

Other objectives

In addition, we will as a scoping exercise, describe the range of all outcome measures reported in all trials. By definition, any included study interventions will fall within the umbrella of physical activity. Therefore, it may be that multiple plausible benefits could emerge that are common to other energy-expenditure interventions.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) including cluster-RCTs. Randomised cross-over studies will be included if data from the first iteration are available and can be analysed as an RCT.

Types of participants

Any stroke survivor, aged 18 years or over, any stroke severity, any stage of care at any time since the stroke. We will include participants regardless of their ability to walk independently or stand independently.

In studies where both stroke and non-stroke participants are included, we will determine whether the subset of data for the stroke participants is accessible from the trial report or through contact with the trial authors. If not, we will exclude the study.

Types of interventions

Interventions

The interventions to be included will have a primary aim of reducing sedentary behaviour, for example interventions to reduce or interrupt sitting time, or both. We will only include RCTs of interventions where a reduction or interruption, or both, of prolonged periods of sedentary behaviour is specifically intended, with or without a co-intervention or usual care.

Examples of interventions could include, but not be limited to: prompting mechanisms to interrupt prolonged sitting, provision of information about health consequences, provision of feedback on behaviour, action planning, restructuring the physical home environment, facilitating walking in place of seated transport, and pharmacological interventions (see [Description of the intervention](#)).

Comparisons

The control intervention will include: 1) usual care; 2) no intervention or waiting-list control; or 3) attention control, sham intervention, or adjunct intervention. The types of comparison are as follows.

- [Interventions to reduce sedentary behaviour] versus [no intervention or waiting-list control]
- [Interventions to reduce sedentary behaviour] versus [attention control, sham intervention or adjunct intervention]
- [Interventions to reduce sedentary behaviour] plus [usual care] versus [no intervention or waiting-list control] plus [usual care]
- [Interventions to reduce sedentary behaviour] plus [usual care] versus [attention control, sham intervention or adjunct intervention] plus [usual care]

Types of outcome measures

A classification of the types of outcome measure in this review is summarised in [Table 1](#).

Primary outcomes

Death

We will record any rate or time to event data.

Recurrent cardiovascular or cerebrovascular events

We will record any rate or time to event data.

Secondary outcomes

Adverse events

In addition to mortality, recurrent cardiovascular and cerebrovascular events, the incidence of falls (and injuries) is the key adverse event to consider. This is because whilst interventions to reduce sitting time could reduce the incidence of falls and fractures, they could also increase the risk ([Growdon 2017](#)).

Sedentary behaviour

Sedentary behaviours, operationalised in terms of amount of sedentary time, obtained with any objective (e.g. accelerometers or inclinometers), self-reported (e.g. questionnaires, diaries) and/or proxy (e.g. screen time, transport time) measures. In addition, some studies may report the degree to which prolonged periods of sedentary behaviour are interrupted or fragmented; there is currently no gold standard for this measurement concept.

This outcome is also an eligibility criterion. We will only include studies if one or more of the following measures of amount or pattern of time spent in sedentary behaviour are included.

Risk factors

Cardiometabolic risk markers, including but not limited to: 1) glucose tolerance, 2) arterial function, 3) blood cholesterol, and 4) blood pressure.

Other outcomes

As a scoping exercise we will be recording (but not analysing quantitatively) all other outcomes reported by the included studies. By definition, any included study intervention will fall within the umbrella of physical activity. Therefore, multiple benefits could arise from this class of intervention that align to common post-stroke problems and include patient-important outcomes ([Pollock 2014](#)). A categorisation of types of other outcomes is included in [Table 1](#).

In studies where more than one measurement tool is used to assess the same outcome (e.g. objective and self-reported measures of sitting time) we will include data in separate meta-analyses or use a sensitivity analysis to determine the effect of the different measurement instruments.

The time points at which outcome data will be collected are 1) at the end of intervention, and 2) the end of follow-up, if available.

Search methods for identification of studies

See the 'Specialized register' section in the [Cochrane Stroke Group](#) module. We will search for trials in all languages and arrange for the translation of relevant articles where necessary.

Electronic searches

We will search the Cochrane Stroke Group trials register and the following electronic databases.

- Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (latest issue)
- MEDLINE Ovid (from 1946 onwards)
- Embase Ovid (from 1974 onwards)
- CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; from 1937 onwards)
- PsycINFO Ovid (from 1806 onwards)
- Conference Proceedings Citation Index- Science (Web of Science; from 1990 onwards)
- PEDro (Physiotherapy Evidence database (www.pedro.fhs.usyd.edu.au/index.html)).

We developed the MEDLINE search strategy ([Appendix 1](#)) with the help of the Cochrane Stroke Group Information Specialist and will adapt it for the other databases. The search strategy includes Cochrane Highly Sensitive Search Strategies for identification of randomised controlled trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions*; [Lefebvre 2011](#)) and Cochrane Stroke Group's search strategies for the identification of 'stroke' studies in respective databases and other resources. These are supplemented with strategies to identify interventions to reduce sedentary time; this is challenging because almost any class of intervention that improves health could plausibly cause a reduction in sedentary time. Therefore, we will search for studies that include search terms relating to 'sedentary behaviours' because these will form part of the description of any study intervention deliberately intended to reduce sedentary time.

In order to identify other published, unpublished and ongoing studies we will search for ongoing trials using the following registries.

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (clinicaltrials.gov/)
- World Health Organization International Clinical Trials Registry Platform (ICTRP) (apps.who.int/trialsearch)
- ISRCTN Registry (www.isrctn.com/)
- Stroke Trials Registry (www.strokecenter.org/trials/)

Searching other resources

We will search for theses using:

- ProQuest Dissertations and Theses Global (www.proquest.com/products-services/pqdtglobal.html);
- British Library EThOS (e-theses online service) (www.ethos.bl.uk);
- DART-Europe E-theses Portal (www.dart-europe.eu/basic-search.php).

We will search grey literature using:

- Google Scholar (scholar.google.co.uk/).

We will check the bibliographies of included studies and perform forward citation tracking of all included trials (and other relevant studies) using Google Scholar (scholar.google.co.uk/) for further references to relevant trials. We will contact researchers in the field (e.g. Sedentary Behaviour Research Network) to obtain additional information on relevant trials and contact original authors for clarification and further data if trial reports are unclear.

Data collection and analysis

Selection of studies

Two review authors (DS or CF or CE or PK) will independently screen titles and abstracts of the unique references obtained as a result of our searching activities. We will exclude trials that two review authors classify as 'exclude'; we will retain all other trials for full-text screening.

We will retrieve the full-text articles for the remaining references and two review authors (DS or CF or CE or PK) will independently screen the full-text articles and identify studies for inclusion, and identify and record reasons for exclusion of the ineligible studies. We will resolve any disagreements through discussion or, if required, we will consult a third person (OV or GM or FVW). We will collate multiple reports of the same study so that each study, not each reference, is the unit of interest in the review.

We will use the Covidence tool (www.covidence.org) to carry out selection process and to record this in sufficient detail to complete 1) a PRISMA flow chart, and 2) a 'Characteristics of excluded studies' table.

We will include studies irrespective of publication status providing available reports have sufficient detail to apply eligibility criteria and perform quality assessment.

We will retain potentially relevant studies with insufficient information to either include or exclude in the 'Studies awaiting classification' table.

Data extraction and management

One review author (DS or CF or CE or PK) will extract data from each included study. The study and outcome data will be entered directly into Review Manager ([RevMan 2014](#)). A second review author (DS or CF or CE or PK) will then cross check all entered data. We will contact study authors to obtain any missing data if required.

The domains for data extraction will include but not be limited to:

- participant details: including age, gender, country of study, type of stroke, time since stroke, stroke severity, ability to stand independently at baseline and ability to walk independently at baseline;

- intervention description: since there is potential for diverse types of intervention we will ensure we record a clear description of the intervention type (sedentary behaviour, physical activity, or part of a multi-component lifestyle intervention), the dose (e.g. time, intensity, frequency and overall programme duration), the intervention setting, the conditions under which the intervention took place (e.g. supervised), and a description of any usual care co-intervention exposure. We will document the intervention parameters using the TIDieR format (Hoffmann 2014);

- comparison intervention: including any usual care exposure;
- outcome measures and data: including frequencies (dichotomous variables) and means and standard deviations (continuous variables) at the end of intervention and at end of follow-up time points. Where required, change from baseline data and other variables which allow imputation of standard deviations will be recorded (e.g. standard error or 95% confidence intervals). We will record the type of outcome tool used to measure sedentary behaviour (objective measurement tool, sitting time self-report, proxy measurement tool);
- risk of bias items.

Assessment of risk of bias in included studies

Two review authors (DS or CF or CE or PK) will independently assess each study using Cochrane's tool for assessing risk of bias (Higgins 2011b). We will resolve any disagreements by discussion or by involving another review author (OV or GM or FVW). We will assess the risk of bias for each of the standard domains in the Cochrane 'Risk of bias' tool with the following exceptions and amendments.

Blinding of participants (performance bias and detection bias)

Participant blinding is often impossible to achieve in behavioural interventions. However, we will consider studies to be at low risk of bias if some attempt was described by the trial authors to disguise the true purpose of the comparisons being made (e.g. describing a trial as a comparison of two different interventions or some kind of 'sham' intervention). We will consider studies to be at high risk of bias if there is an imbalanced exposure such as would occur with no control intervention or a waiting-list control.

Incomplete outcome data (attrition bias)

This domain will be assessed twice, once at the end of intervention and once at the end of follow-up. We will consider studies to be at high risk of bias where imbalanced losses were judged to have occurred coupled with a per-protocol analysis. If overall participant attrition is 20% or greater of those randomised, we will consider a

trial at high risk of bias (Schulz 2002), irrespective of distribution of losses, reasons given or analytical approach (e.g. imputations, intention-to-treat).

Other bias

We will consider 'Risk of bias' items relevant to cluster-RCTs in this domain.

Imbalanced exposures

We will include this additional 'Risk of bias' item because an imbalanced exposure could exaggerate benefits (or harms) in a way where it is impossible to separate the effects of the intervention content from the effects of attention. Therefore, strictly speaking, this is a confounding effect rather than a bias effect, but it is appropriate to record it and analyse it in the same way as other of bias items. We will consider studies to be at low risk of bias if a 'dose' of exposure or attention was provided in the control group which matched that in the intervention groups (e.g. attention control or sham intervention). We will consider studies to be at high risk of bias if the control group receives no control intervention including being allocated to a waiting-list control.

In all categories when there is insufficient information to assign either a 'low risk' or 'high risk' of bias, we will contact the trial authors and ask them for clarification. Where missing supplementary information cannot be obtained we will record an 'unclear' risk of bias. We will record 'high', 'low' or 'unclear' risk of bias along with a descriptive justification for our judgment in the 'Risk of bias' tables. The data will be presented in 'Risk of bias' summary graphs.

Measures of treatment effect

Dichotomous data

For dichotomous outcome data we will calculate odds ratios (OR) and 95% confidence intervals (CIs).

Continuous data

Where possible, we will present the effects of interventions on all continuous outcome data as a mean difference (MD) and 95% CIs. In instances where different scales are used to measure the same clinical outcome, we will present the data as standardised mean difference (SMD) and 95% CIs.

Unit of analysis issues

Cluster-RCTs trials: if clustering as a unit of allocation was not controlled by the trial authors, we will implement this, where appropriate, during meta-analysis using the methods described in the Cochrane Handbook (Higgins 2011a).

Crossover studies: the data can be truncated after the first iteration of a crossover study and treated as an RCT. We will ignore subsequent iterations because of the risk of carry-over effects.

Lag-control or waiting-list trials: we will deal with these in the same way as crossover studies. We will ignore the delayed or waiting-list iteration of the study because of the risk of carry-over effects.

In studies with more than one relevant control group, we will use only one control group within a meta analysis. We will perform sensitivity analysis to examine the relative influence of selecting each group on meta-analysis results. Where data from multiple control groups are similar we will consider combining the control group data using the methods described in the *Cochrane Handbook or Systematic Reviews of Interventions* (Higgins 2011a).

In studies with more than one relevant intervention group, we will include all intervention groups as separate comparisons within a meta-analysis, with the control group data replicated across all comparisons, but with the control group sample size divided evenly across among the comparisons to prevent inflation of overall sample size.

The principal time points for outcome measurement are: 1) at the end of intervention, and 2) at the end of follow-up.

Dealing with missing data

Missing participants: we will account for the nature and extent of missing participant data (e.g. losses to follow-up) and how this was dealt with by the trial authors (e.g. intention-to-treat analysis) via one of the 'Risk of bias' assessments ([Assessment of risk of bias in included studies](#); Incomplete outcome data).

Incomplete reporting: If RCTs have missing information we will contact the trial authors to request this. If there is insufficient information to include or exclude a potentially-relevant trial and this cannot be retrieved then we will retain the trial in the 'Studies awaiting classification' section in case the information emerges at a later date.

Assessment of heterogeneity

We will assess heterogeneity using the I^2 statistic presented as part of the forest plots in [RevMan 2014](#). We will interpret values of I^2 exceeding 50% as indicating substantial heterogeneity. In these cases we will investigate potential causes of variation by inspecting study effects and by using subgroup and sensitivity analysis if appropriate.

Assessment of reporting biases

The comprehensive search strategy will help ameliorate reporting biases.

When meta-analyses include a minimum of 10 studies, we will use a funnel plot (treatment effect versus trial size).

Data synthesis

Where we consider studies to be sufficiently similar, we will conduct a meta-analysis by pooling the appropriate data using [RevMan 2014](#).

We will use random-effects meta-analysis models to calculate measures of effect and 95% CIs at the end of intervention and the end of follow-up for each outcome measure with sufficient suitable data to pool.

We will use GRADE to assess the evidence for the primary outcomes of death and recurrent events, plus the secondary outcomes of adverse events and sedentary behaviour; these analyses will be performed and presented in a 'Summary of findings' table ([Table 2](#)) generated using GRADEpro GDT software ([gradepro.org/](#)). The 'Summary of findings' table will include the primary outcomes (death and recurrent events), plus the secondary outcomes of adverse events and sedentary behaviour

Subgroup analysis and investigation of heterogeneity

We will obtain all the data to allow subgroup categorisation at the point of data extraction. We will perform pre-planned subgroup analysis when there are five or more RCTs within one meta-analysis comparison which can be partitioned into subgroups based on the following criteria.

- Time since stroke (acute, chronic)
- Ability to stand at baseline (independent, requires assistance)
- Ability to walk at baseline (independent, requires assistance)
- Intervention duration (< 3 months, ≥ 3 months)
- Intervention type (reduce sedentary time, interrupt sedentary time, reduce and interrupt sedentary time)

The subgroups may indicate informally whether study level characteristics (of participant and intervention) are connected to study effects sizes and are potentially introducing a source of heterogeneity into pooled effect sizes.

Sensitivity analysis

We will use sensitivity analyses to examine the effect of decisions made during the review process.

- Effect of including cluster-RCT data
- Effect of more than one relevant control group
- Effect of more than one measurement tool for the same outcome
- Effect of including study data imputed by the review authors

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* Indicates the major publication for the study

ADDITIONAL TABLES**Table 1. Outcome measures classification**

Outcome		Type or Domain
Primary outcomes	Death ¹	Any cause
	Recurrent non-fatal events ¹	Cardiovascular
		Cerebrovascular
Secondary outcomes	Adverse events ¹	Falls
	Sedentary behaviour ¹	Time
		Pattern
Other outcomes	Risk factors	
	Impairments	Physical fitness
		Balance
	Activity limitations	Specific
		Generic

Table 1. Outcome measures classification (Continued)

	Participation restriction
	Quality of life
	Psychosocial
	Mood
	Fatigue
	Cognition
	Complications of immobility

1 Outcome categories to be included in the 'Summary of findings' table

Table 2. 'Summary of Findings' table outline

Participants: people with stroke, who participated in an intervention to reduce or fragment sedentary time Setting: Any Intervention: Any intervention designed to reduce or fragment sedentary behaviour with or without usual care Comparison: No intervention, attention control, sham intervention or adjunct intervention with or without usual care						
Outcomes	Absolute risk	Comparative risk (95% CI)	Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
Death ¹						
Recurrent events ²						
Adverse events ³						
Sedentary behaviour ⁴						

CI: Confidence Interval, GRADE: Grades of evidence as per Grading of Recommendations Assessment, Development and Evaluation Working Group

1 Death by any cause

2 Non-fatal cerebrovascular or cardiovascular events

3 Number of falls

4 Wake time spent lying/sitting/reclining or degree of fragmentation of sedentary time, recorded by any tool.

APPENDICES

Appendix I. MEDLINE search strategy

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ or stroke, lacunar/ or vasospasm, intracranial/ or vertebral artery dissection/
2. (stroke or poststroke or post-stroke or cerebrovasc\$ or brain vasc\$ or cerebral vasc\$ or cva\$ or apoplex\$ or SAH).tw.
3. ((brain\$ or cerebr\$ or cerebell\$ or intracran\$ or intracerebral) adj5 (isch?emi\$ or infarct\$ or thrombo\$ or emboli\$ or occlus\$)).tw.
4. ((brain\$ or cerebr\$ or cerebell\$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage\$ or hemorrhage\$ or haematoma\$ or hematoma\$ or bleed\$)).tw.
5. hemiplegia/ or exp paresis/
6. (hemipleg\$ or hemipar\$ or paresis or paretic).tw.
7. or/1-6
8. Lifestyle/ or Sedentary Lifestyle/
9. Posture/
10. Motor activity/
11. ((uninterrupted or long\$ or prolong\$ or extend\$ or bout or continu\$ or protracted or sustain\$ or period\$ or duration\$ or time\$) adj5 (posture or sitting or sit or sat or seat\$ or lying)).tw.
12. (sedentar\$ or stationary or nonexercise or non-exercise or inactiv\$ or reclin\$).tw.
13. ((screen\$ or transport\$ or travel\$ or car\$ or train\$ or bus or buses or media or indoor\$ or desk\$) adj3 (time\$ or period\$ or duration\$)).tw.
14. or/8-13
15. randomized controlled trial.pt.
16. controlled clinical trial.pt.
17. randomized.ab.
18. placebo.ab.
19. randomly.ab.
20. trial.ab.
21. groups.ab.
22. or/15-21
23. 7 and 14 and 22

WHAT'S NEW

Date	Event	Description
11 April 2018	Amended	Minor corrections to the references

CONTRIBUTIONS OF AUTHORS

All authors had an active role in the protocol design, writing, and editing.

DECLARATIONS OF INTEREST

D Saunders: none known.

C Fitzsimons: none known.

P Kelly: none known.

O Verschuren: none known.

C English: none known.

GE Mead has received research funding for exercise after stroke. She has received honoraria from Later Life Training to develop an educational course of exercise after stroke for exercise professionals. She has also received honoraria and expenses to present work on exercise after stroke at conferences.

F van Wijck has received grants from Chest Heart Stroke Scotland, Edinburgh Leisure, NHS Greater Glasgow, and the Scottish Executive. She was a member of the team that developed the “Exercise after Stroke Specialist Instructor Training Course”, which was licensed to Later Life Training (LLT) in 2010. All proceeds have been going into funding further research in this area.

SOURCES OF SUPPORT

Internal sources

- New Source of support, Other.

External sources

- No sources of support supplied